

Figure 2—Mass spectrum of II.

acid derivatives by the action of a nucleophilic reagent.

A preliminary screening in mice using intraperitoneal administration suggested that the new compound produces skeletal muscle relaxation.

#### EXPERIMENTAL

To a solution of 1.84 g (0.01 mole) of 5,5-diethyl-2-thiobarbituric acid in 50 ml of absolute ethanol was added 2.6 g (0.03 mole) of silver oxide. The suspension was refluxed for 24 hr. After cooling and adding 2.5 g of talcum to adsorb excess silver oxide and silver sulfide, the mixture was filtered, the filtrate was evaporated to dry-

ness, and the residue (1.9 g) was purified by TLC on silica gel with a solvent mixture of acetone-chloroform (1:9),  $R_f$  0.37, corrected mp 77°.

The IR spectrum of II in chloroform showed two CO absorption bands at 1735 and 1700  $\text{cm}^{-1}$  as well as a strong CN absorption at 1590  $\text{cm}^{-1}$ . The spectrum taken in a KBr pellet is presented in Fig. 1. The NMR spectrum of II in deuteriochloroform showed a badly resolved triplet of the NH proton at 1.02 ppm ( $\tau$ ); the quadruplets and the triplets of the ethoxy groups at 5.44 and 8.59 ppm, respectively; and the two ethyl groups at 7.98 and 9.16 ppm. In the mass spectrum (Fig. 2) were found the molecular ion peak at  $m/e$  212 (calc. mol. wt. 212.26) and the usual pattern of fragmentation of the barbituric ring (7) with ion fragments resulting from the loss of a first ethylene molecule at  $m/e$  156 and of an ethylisocyanate molecule at  $m/e$  141.

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## New Compounds: Unusual Chlorination of 2,3-Dimethyl-1,2,4-benzothiadiazine 1,1-Dioxide

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**Abstract** □ Chlorination of 2,3-dimethyl-1,2,4-benzothiadiazine 1,1-dioxide and its 6-chloro derivative with chlorine in dimethylformamide yielded a C-chlorinated end-product.

**Keyphrases** □ 2,3-Dimethyl-1,2,4-benzothiadiazine 1,1-dioxide—unusual chlorination in dimethylformamide yielding a C-chlorinated end-product □ Chlorination—2,3-dimethyl-1,2,4-benzothiadiazine 1,1-dioxide in dimethylformamide yielding a C-chlorinated end-product

The reported chlorination (1, 2) of 3-alkyl-2H-1,2,4-benzothiadiazine 1,1-dioxide (I) yields the corresponding 7-chloro derivative (II). Similarly, 3-oxo-3,4-dihydro-1,2,4-benzothiadiazine 1,1-dioxide (III) yields a 7-chloro derivative (IIIa) or a 5,7-dichloro derivative (IIIb), depending on the reaction conditions.

This note reports the unexpected side-chain chlorination of 2,3-dimethyl-1,2,4-benzothiadiazine 1,1-

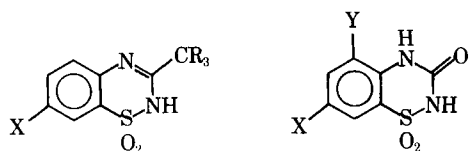
dioxide (IV), which did not undergo ring chlorination but, in fact, yielded the corresponding 3-trichloromethyl derivative (IVa). Similarly, V yielded Va.

It was reported (2, 3) that a rearrangement due to the conversion of *N*-chloramines [the Orton reaction (4)] is possible with I and III. This yields a C-chlorinated end-product from the *N*-chloro intermediate.

Since such an intermediate is not possible in compounds of type IV, the present investigation suggests that the chlorination of these compounds in dimethylformamide undergoes a similar course of reaction as that of toluene or methylpyridine (5) when chlorinated with molecular chlorine.

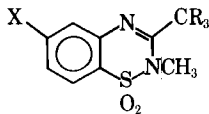
#### EXPERIMENTAL

**2-Methyl-3-trichloromethyl-1,2,4-benzothiadiazine 1,1-Dioxide (IVa)**—Compound IV (6) (4 g) was dissolved in 14 ml of dimethylformamide. Chlorine was slowly added to the stirred solution at 45°. As soon as 4 g of chlorine was absorbed, the gas inlet



I: R = alkyl, X = H  
 II: R = alkyl, X = Cl

III: X = H, Y = H  
 IIIa: X = Cl, Y = H  
 IIIb: X = Cl, Y = Cl



IV: R = H, X = H  
 IVa: R = Cl, X = H  
 V: R = H, X = Cl  
 Va: R = Cl, X = Cl

was removed and the dark-yellow solution was allowed to stand for 0.5 hr. The reaction mixture was then poured into crushed ice and the solid material was collected and washed several times with water. Recrystallization from methanol gave crystals, mp 135–137°. NMR analysis in acetone-*d*<sub>6</sub> gave a proton count of seven, showing the four protons for the benzene ring at 8 ppm and a singlet (three protons) at 3.75 ppm for the methyl group in the 2-position.

*Anal.*—Calc. for C<sub>9</sub>H<sub>7</sub>Cl<sub>3</sub>N<sub>2</sub>O<sub>2</sub>S: C, 34.47; H, 2.25; N, 8.93. Found: C, 34.86; H, 2.21; N, 8.95.

**6-Chloro-2-methyl-3-trichloromethyl-1,2,4-benzothiazine 1,1-Dioxide (Va)**—Compound V (16 g) was chlorinated in 50 ml of dimethylformamide at 55–80° with 16 g of chlorine. Recrystallization of the crude substance from benzene–hexane gave Va, mp 145–146°. NMR analysis in acetone-*d*<sub>6</sub> showed a singlet at 3.75 ppm for the methyl group and three protons for the ring at 7.75–8.20 ppm.

*Anal.*—Calc. for C<sub>9</sub>H<sub>6</sub>Cl<sub>4</sub>N<sub>2</sub>O<sub>2</sub>S: C, 31.06; H, 1.74; N, 8.05. Found: C, 31.23; H, 1.92; N, 7.81.

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## COMMUNICATIONS

### Hydroxymethylfuraldimines: Possible Intermediates in Maillard Reaction

**Keyphrases** □ Hydroxymethylfuraldimines—possible intermediates in Maillard reaction, relationship to browning of dextroamphetamine sulfate □ Dextroamphetamine sulfate—hydroxymethylfuraldimines as possible intermediates in Maillard reaction □ Maillard reaction—hydroxymethylfuraldimines as possible intermediates, relationship to browning of dextroamphetamine sulfate

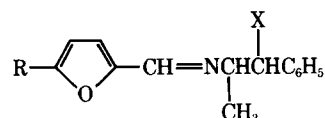
To the Editor:

Recently, Blaug and Huang (1) reported that dextroamphetamine sulfate yields a brown precipitate when heated with dextrates in solution. This brown precipitate was postulated as the imine (Ia) resulting from condensation of amphetamine with 5-hydroxymethylfurfural on the basis of elemental analysis, a strong band at 1650 cm<sup>-1</sup> in the IR spectrum, and TLC.

During investigations conducted in this laboratory, it became of interest to prepare Ia and a few other 2-

furanecarboxaldimines (Ib–Id) for spectral and reactivity comparisons. These compounds were readily prepared by warming benzene (Ib–Id) or ethanol (Ia) solutions of the amine and the furfural and were unambiguously characterized by their IR, UV (Table I), and NMR spectra<sup>1</sup> (Figs. 1a–1d). Compounds Ib–Id were readily purified by either vacuum distillation (Ic) or crystallization (Ib and Id).

Since extensive decomposition of Ia occurred on attempted distillation, the method of choice for its preparation involved employing a slight excess of



	R	X
Ia:	CH <sub>2</sub> OH	H
Ib:	CH <sub>2</sub> OH	OH
Ic:	H	H
Id:	H	OH

<sup>1</sup> Determined on a Varian T-60 or Varian XL-100.